

Compression and walking versus bed rest in the treatment of proximal deep venous thrombosis with low molecular weight heparin

Hugo Partsch, MD,^a and Werner Blättler, MD,^b *Vienna, Austria, and Zurich, Switzerland*

Objective: The purpose of this randomized controlled trial was to evaluate the benefits of compression and walking exercises in comparison with bed rest in the acute stage of proximal deep venous thrombosis (DVT).

Methods: Forty-five patients with proximal DVT that was proved with compression ultrasound scan or phlebography were randomized into three groups. Group A consisted of 15 patients who received inelastic compression bandages (Unna boots on the lower leg, adhesive bandages on the thigh), and group B consisted of 15 patients who received thigh-length compression stockings, class II. Group C consisted of 15 patients who underwent bed rest and no compression. All patients received dalteparin, 200 IU/kg per body weight, subcutaneously every 24 hours. The clinical characteristics of the three groups were comparable. Primary end points were the reduction of pain assessed daily with the Visual Analogue Scale and the Lowenberg test, the reduction of leg circumference at the ankle and calf levels, and the improvement of clinical scores. The daily walking distance was measured with a pedometer. Safety parameters were ventilation-perfusion scans and duplex ultrasound scans performed on days 0 and 9.

Results: The daily walking distance was between 600 and 12,000 m in the compression groups and averaged 66 m in the bed rest group. The pain level showed a statistically significant reduction starting after the second day in the compression groups (A and B) and after 9 days in the bed rest group C ($P < .05$). The same was true for the measurement of leg circumference. Improvement of the clinical scores was significantly better in the compression groups compared with the bed rest group ($P < .01$). There was no significant difference concerning the occurrence of new pulmonary emboli and regression of thrombus diameter. Progression of thrombi in the femoral vein was greater and occurred more frequently in the bed rest group than in the other two groups ($P =$ not significant).

Conclusion: Mobile patients with acute proximal DVT treated with low molecular weight heparin should be encouraged to walk with compression bandages or medical compression stockings. The rate of resolution of pain and swelling is significantly faster when the patient ambulates with compression. The risk of pulmonary embolism is not significantly increased by this approach. (J Vasc Surg 2000;32:861-9.)

From the Dermatological Department, Wilhelminenspital,^a and Angio Bellaria.^b

Competition of interest: nil.

Supported by a grant of the German Society of Phlebology.

Presented at the Twelfth Annual Meeting of the American Venous Forum, Phoenix, Ariz, Feb 3-6, 2000.

Reprint requests: Hugo Partsch, MD, Professor of Dermatology, Wilhelminen Hospital, A 1171 Vienna, Austria (e-mail: Hugo.Partsch@der.wil.magwien.gv.at).

Copyright © 2000 by The Society for Vascular Surgery and The American Association for Vascular Surgery, a Chapter of the International Society for Cardiovascular Surgery.

0741-5214/2000/\$12.00 + 0 24/6/110352

doi:10.1067/mva.2000.110352

Conventionally, deep venous thrombosis (DVT) is treated with an intravenous infusion of unfractionated heparin for at least 5 days, followed by a course of oral anticoagulants. Hospital admission and bed rest for the duration of intravenous infusions have been recommended with the goal of avoiding leg movement to protect patients from pulmonary embolism. This traditional management of DVT has changed considerably since the approval of subcutaneous administration of low molecular weight heparins (LMWHs) for the treatment of DVT. The new approach includes home treatment in selected cases.^{1,2} Patients and their

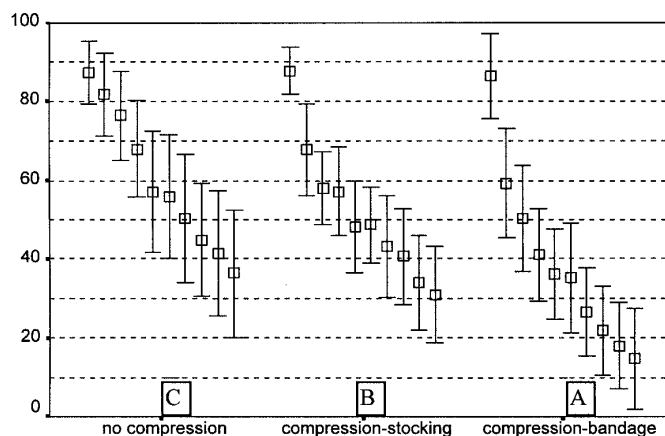


Fig 1. Intensity of pain during the 9-day treatment period for each of the three groups measured with VAS (100 mm = maximal degree of pain, mean \pm SD). In the compression groups significant differences compared with day 0 start on day 1; in the bed rest group differences start on day 5. Analysis of variance of day 9 under control of day 0: groups A/B, A/C, B/C, not significant ($P = .06$).

relatives are instructed in the subcutaneous administration of these new drugs, but specific guidelines regarding the patient's ambulation are lacking. Questions that include whether these individuals should stay in bed, walk around, or wear any leg compression devices are not routinely addressed.

In several prospective cohort studies in which consecutive patients with DVT were investigated with repeated lung scanning, we were able to demonstrate that there is no increased danger of pulmonary embolism if mobile patients are treated with LMWH and keep walking with compression bandages regardless of the size or location of the thrombi.³⁻⁵ These findings have been confirmed by recent randomized studies in which bed rest is compared with compression and walking.^{6,7}

It has been our experience for many years that patients with DVT recover much faster when they are encouraged to walk with firm compression bandages. However, until now, evidence-based data proving the advantages of active walking exercises with compression have been lacking. This article presents preliminary results of a randomized controlled trial in which bed rest is compared with walking exercises and compression.

METHODS

Study design. This study is a randomized, unblinded, controlled trial in which three groups of adjuvant treatment modalities in patients with acute, symptomatic proximal DVT are compared:

- Inelastic Unna boot bandages + walking exercises

(group A)

- Elastic compression stockings + walking exercises (group B)
- Bed rest and no compression (group C)

The trial was designed as a multicenter study and approved by the local Institutional Review Boards at each center. The following data represent the results from an interim analysis and have been collected entirely from the center in Vienna. Since this manuscript was originally presented, eight more patients have been enrolled.

Patients. We considered 148 consecutive mobile patients older than 18 years with proximal DVT (thrombosis of the popliteal or more proximal deep veins of the legs) that was documented with compression ultrasound scan or phlebography for enrollment in the study. The duration of symptoms had to be less than 14 days. Patients were excluded from the study if compression or heparin therapy had already started, if there was an indication for thrombolysis or thrombectomy, and if they had massive symptomatic pulmonary embolism or severe concomitant diseases. They were also excluded if the ankle-brachial Doppler scan index was lower than 0.8, if they were pregnant or breast-feeding, or if there was a contraindication for compression, anticoagulation, or both. Randomization was performed with sealed envelopes, allocating 15 patients into each treatment group for an interim analysis.

Anticoagulation was started in each patient immediately after proximal vein thrombosis had been documented objectively by color-coded duplex

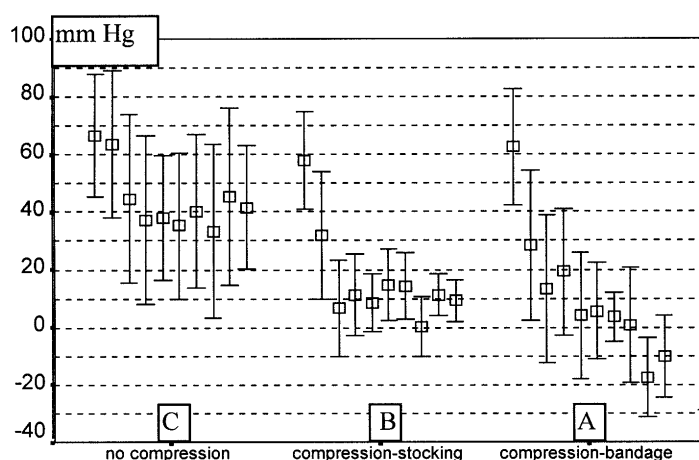


Fig 2. Degree of discomfort assessed with Lowenberg test for each patient in which the normal leg was compared with the involved leg. The differences between the findings in the normal versus the affected leg for each patient are depicted (mean \pm SD). Statistically significant improvement compared with day 0 is reached in groups A and B on day 2. In group C there is no significant difference up to day 9. Analysis of variance of day 9 under control of day 0: A/C, $P < .001$; A/B and B/C, $P < .01$.

scan imaging with compression. Additional contrast phlebography was used in 3 patients, isotopic phlebography in 11, and magnetic resonance imaging phlebography in 10.

Treatment regimens. All patients received subcutaneous injections of dalteparin (Fragmin), 200 IU/kg per body weight, once every 24 hours for a minimum of 6 days (mean, 8.5 ± 0.9 days). They also received overlapping oral anticoagulants (Marcoumar) with doses adjusted to reach international normalized ratio values between 2.0 and 3.0.

In *group A*, tight Unna boot bandages (Varicex F zinc plaster, 10 cm \times 10 m) were applied on the lower leg and covered with a short-stretch bandage (Rosidal K, 10 cm \times 5 m). The mean pressure on the distal lower leg, which was measured with an Oxford pressure monitor in several patients, was 50 mm Hg. An adhesive short-stretch bandage (Panelast, 10 cm \times 5 m) was applied with considerable pressure over the knee and up to the groin. This bandage was changed every 3 days.

Group B received ready-made thigh-length compression stockings, class II (Sigvaris 503), which were adapted to the individual leg size. They were worn both day and night. Both groups were encouraged to walk as much as possible on the ward and on the hospital grounds.

In *group C*, compression bandages were started only after the ninth day. Patients were advised to stay in bed, but were allowed to get up to use the toilet.

The daily walking distances were measured with a pedometer in each group.

End points and outcome measures. During the 9 days of the study, patients underwent several examinations. These included daily measurements of walking distance with a pedometer and of the pain level, which was assessed with the Visual Analogue Scale (VAS) and the bilateral Lowenberg test.⁸ On days 0, 3, 6 and 9, clinical scores and leg circumference were measured. Additional study-related investigations performed on days 0 and 9 included compression sonography and ventilation-perfusion (V/Q) lung scans.

The changes in pain, of leg circumference, and of the clinical scores were chosen as *primary end points*. The occurrence of new pulmonary emboli compared with a baseline scan and changes of thrombus extension in the femoral vein were taken as safety parameters.

Pain was assessed daily at the same time with two methods: The spontaneous sensation of pain was assessed by the patient on a VAS and in a more objective way with a modified Lowenberg test.⁹ A cuff was applied on each calf without removing bandages or stockings. Pressure was applied, and the value at which the patient perceived pain in each calf was recorded. The measurements were repeated within a few minutes, and the mean value was calculated. The difference between the thrombosed and the healthy leg was calculated and used for analysis.

Table I. Baseline characteristics of patients according to treatment group

	Group A: Unna boot (n = 15)	Group B: compression stocking (n = 15)	Group C: bed rest, no compression (n = 15)
Age (y)	59.2 ± 19.80	61.7 ± 19.23	52.2 ± 16.87
Weight (kg)	80.53 ± 11.08	80.0 ± 15.52	86.0 ± 10.8
Female/male	7/8	5/10	4/11
	No./total no.(%)		
Most proximal thrombi pelvis/cava	2/0 (13.3/0)	5/1 (33.3/6.6)	4/1 (26.6/6.6)
Left side	11 (73)	8 (53)	9 (60)
Previous DVT			
Same leg	3 (20)	3 (20)	1 (6.7)
Contralateral leg	4 (26.7)	3 (20)	4 (26.7)
Previous surgery	1 (6.7)	1 (6.7)	1 (6.7)
Immobility, trauma	5 (33.3)	8 (53.3)	7 (46.7)
Travel	3 (20)	4 (26.7)	1 (6.7)
Cancer	3 (20)	2 (13.3)	0
Oral contraceptives	1 (6.7)	1 (6.7)	3 (20)
Dyspnea at admission	4 (26.7)	3 (20)	3 (20)

Clinical scores were calculated for the following seven symptoms: (1) pain during walking, (2) painful foot sole, (3) painful calf palpation, (4) subfascial edema, (5) prefascial edema, (6) increase of skin temperature, and (7) redness/cyanosis. The severity score comprised four stages (absent, mild, marked, and severe) so that a maximal score of 28 could be reached. *Prefascial edema* was defined as a palpable indentation of the skin after firm pressure was applied for more than 10 seconds by the thumb. An increase of the consistency of the calf palpated in a relaxed lying position of the patient was defined as *subfascial edema*. Circumference of the lower leg was measured at the ankle and at midcalf level.

We measured the distance of the tip of the thrombus from the saphenofemoral junction with compression sonography (Diasonics VST Master Series; Milipita, Calif) in those cases where thrombi did not extend into the pelvis. The largest diameter of the clot during compression and the largest diameter of the vein were measured 10 cm below the tip of the thrombus or, in cases with iliac involvement, from the groin. By scanning down the superficial femoral vein in a transverse view using compression maneuvers with the duplex scan probe, we located the tip of the thrombus at the site of decreased compressibility.

Perfusion lung scans with technetium-99m-labeled microspheres were performed, with ventilation scans with labeled aerosols in case of perfusion defects. The assessment of compression ultrasound scan and of V/Q scans was performed by observers who were unaware of the patient's treatment. Complete blood counts were obtained twice weekly.

Statistical analysis. According to the results of a previous study,^{9,10} the statistical power was calculated as 71% and 65%, respectively, for a sample size of 60 and a two-sided 5% significance level for the mean values of the differences in the VAS pain scale and the Lowenberg test. For the analysis of treatment effects, analysis of variance was calculated. For nominal data, the Pearson and the χ^2 tests were calculated.

RESULTS

Patients

Of 148 eligible patients admitted because of proximal DVT between August 1998 and August 1999, 45 gave written consent to participate in this study. The baseline characteristics of the treatment groups were similar (Table I).

Table II shows the average daily walking distance in the three groups. The walking distance varies between 500 and 12,000 m in the compression groups and is significantly higher than in the bed rest group.

Primary end points

Pain. The degree of spontaneous pain as documented by VAS in the three treatment groups is shown in Fig 1. In groups A and B, pain levels, compared with day 0, start to be significantly lower already on day 1; in group C, the levels are lower on day 5. The use of bandages seems to have a more pronounced effect than the use of stockings.

The Lowenberg test assesses a more specific perception of pain. The difference in the readings

Table II. Daily walking distance in meters measured with pedometer (mean \pm SD)

	Group A: Unna boot	Group B: compression stocking	Group C: bed rest, no compression	Statistical difference
Walking distance, day 0	1793.0 \pm 1425.0	2058.0 \pm 1649.0	66.0 \pm 112.1	A/C, $P < .001$; B/C, $P < .001$
Walking distance, day 9	4048.5 \pm 2947.0	3659.9 \pm 2905.0	179.3 \pm 160.6	A/C, $P < .001$; B/C, $P < .001$

between the healthy and the diseased leg is shown in Fig 2. The reduction of pain is slight without compression, and there is no further decrease during the subsequent 7 days of bed rest. Compression with stockings leads to rapid and almost complete relief. Compression with bandages has the same initial effect but continues to improve contrary to the other treatment groups. Statistically significant differences, compared with day 0, are reached in groups A and B on day 2. In group C, there is no significant difference up to day 9.

Leg circumference. The differences between the circumferences of the diseased leg and the healthy leg at the ankle and at calf level give an objective parameter for the edema caused by DVT. On day 9 the reduction of swelling is significantly more pronounced in the compression groups compared with the bed rest group (Table III). The decrease of the circumference at calf level is more pronounced in group A, whereas there is no difference between Unna boot and stockings at the ankle level.

Clinical scores. In both compression groups, the clinical score is significantly improved. The score is more pronounced with Unna boots than with compression stockings (Table III).

Safety parameters

Lung scans and duplex scans. No significant differences are found concerning the frequency of new pulmonary emboli, all clinically silent, and the thrombus diameter measured with duplex scan. The rate and amount of thrombus extension or regression in patients with DVT in the femoral vein are shown in Fig 3. Thrombus progression is observed in 4 (31%) of 13 patients in the Unna boot group, in 1 (11%) of 9 patients in the stocking group, and in 4 (40%) of 10 patients in the bed rest group. The longest extension of the thrombi is found in the bed rest patients. All these changes are not statistically significant.

Side effects. Three patients in the Unna boot group (20%) and five patients in the stocking group (33.3%) reported local pain due to friction or showed irritation of the skin. In no case was this a cause to stop treatment. No major bleeding complications or relevant changes of blood count were observed.

DISCUSSION

The results of several controlled trials suggest that subcutaneous LMWH in selected, uncomplicated patients with DVT is as safe and effective as intravenous unfractionated heparin, and that most patients can be treated as outpatients or discharged early.^{1,2} Similar conclusions were also drawn from studies in which patients with pulmonary embolism were included.^{11,12} The amount of physical activity of the patients is not addressed in any of these studies. Outpatient guidelines include patient counseling regarding LMWH injections and oral anticoagulation, but no specific advice regarding leg compression and ambulation is available to the patient. One important study demonstrated that compression stockings are able to dramatically reduce the frequency of the post-thrombotic syndrome some years after proximal DVT, but compression therapy was started only several days after hospital admission.¹³

There is an old tradition in continental Europe to treat mobile patients who have acute DVT with compression bandages and walking exercises. As early as 1910 and years before heparin was discovered, Heinrich Fischer¹⁴ recommended zinc plaster bandages, which he learned about from his teacher Unna, to treat patients with thrombosis, speculating that firm external compression would affix the clots to the vein wall. This idea is also the reason why in this study, continuous daylong and nightlong compression of the whole leg was performed, both with bandages and stockings. We do not know if in the future calf stockings worn only during daytime will perhaps reveal similar results.

It has been our routine for many years not to immobilize patients with acute proximal DVT as long as they are mobile, regardless of size, extent, or morphology of the thrombi. Compared with data in the literature that are based on bed rest, we found that even patients with iliofemoral DVT did not have a higher risk of scintigraphic or fatal pulmonary embolism if treated with compression, walking exercises, and either unfractionated heparin given subcutaneously³ or LMWH.^{4,5,10} These findings were recently confirmed by two randomized controlled trials that showed no statistically significant differ-

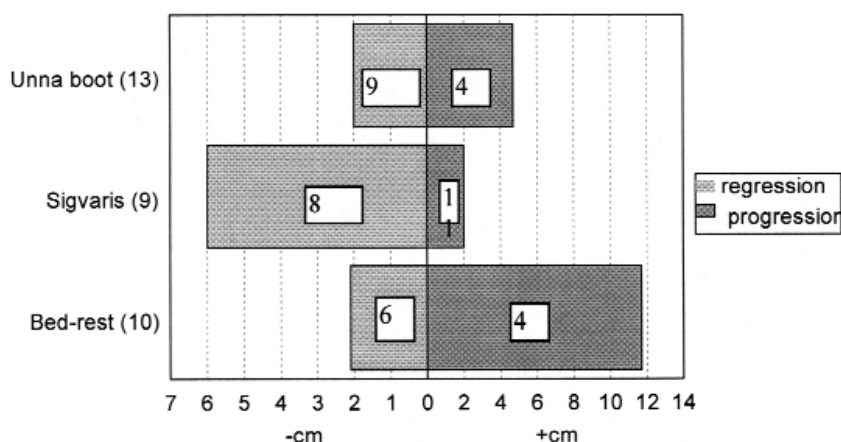


Fig 3. Change of thrombus length in the femoral vein (cm) measured with duplex sonography. The *digits* in the bars reflect the number of patients showing regression (*left*) or progression (*right from the center*).

ences of the rate of new pulmonary emboli between bed rest and walking with compression in 129 and 122 patients, respectively.^{6,7}

However, most centers, up to now, recommended bed rest because of the fear of pulmonary embolism. No controlled study has been available until today that compared safety and efficacy of these two management modalities.

All eligible patients received detailed information concerning the nature of this trial, including the risks associated with a 9-day period of bed rest. It was possible to enroll only one third of the eligible patients after they understood the nature of this trial. Two thirds were not willing to undergo bed rest for 9 days.

Our results of this study indicate that compression and walking exercises reduce pain and swelling in patients with proximal DVT much faster and more effectively than bed rest does without a greater risk of pulmonary embolism. With VASs (Fig 1) and the Lowenberg test (Fig 2), our results show that after 4 days the average pain level after compression with Unna boots is in the same range as for the bed rest group after 9 days. Bandages are more effective than compression stockings. However, compression stockings also lead to a significantly faster and more extensive pain reduction than does bed rest.

Pain results from an increase of compartmental pressure resulting from congestion of muscle veins by thrombi and trapped blood. It is generally thought that pain is reduced if the thrombosed leg is immobilized. Because the spontaneous decrease of compartmental pressure is slow, a rapid relief of inducible pain, assessed with the Lowenberg test, cannot be expected. External leg compression—in conjunction with walk-

ing—leads to a palpable reduction of subfascial consistency that is probably due to a lowering of compartmental pressure and thus to a decrease of pain. Indirect support for this assumption is that the decreased subfascial lymph transport in patients with DVT and with post-thrombotic syndrome is enhanced by firm external compression.¹⁵ Pain assessed with VAS decreased more slowly than pain monitored with the Lowenberg test. Compression with stockings has a somewhat less sustained effect than compression with bandages. We speculate that phenomena other than compartmental pressure (eg, inflammatory processes) may play a role. Compression with firm, inelastic bandages has a greater effect on such phenomena than compression with elastic hosiery.

A statistically significant decrease in the degree of leg swelling was observed in the compression and walking groups. After 9 days, measurable edema disappeared completely in the bandage group. A significant reduction of the circumference of the leg with DVT, which is remarkably extensive in the ankle area, is also observed after compression stockings.

Both pain and swelling are important parameters, especially for the patients' perception of their disease. The same is true for the clinical scores, which also showed a significantly superior course of regression for the compression groups compared with the bed rest group.

Baseline lung scans did not show significant differences among the treatment groups. Only a few patients (10) reported some degree of dyspnea during walking. Most of the pulmonary emboli that were proved with scintigraphy were therefore clinically silent. The occurrence of new emboli detected by the second lung scan was not significantly differ-

Table III. Differences in circumference between the two legs at ankle and calf level (cm), clinical scores, V/Q scan, and thrombus diameter on days 0 and 9 (mean \pm SD)

	Group A: <i>Unna boot</i>	Group B: <i>stocking</i>	Group C: <i>bed rest</i>	Statistical difference
Difference of circumference, ankle, day 0	1.40 \pm 1.33	1.93 \pm 1.53	1.47 \pm 1.03	ns
Difference of circumference, ankle, day 9	-0.27 \pm 0.82	-0.30 \pm 0.80	1.20 \pm 1.28	A/C, $P < .001$, B/C, $P < .001$, A/B, ns
Difference of circumference, calf, day 0	3.17 \pm 1.81	2.93 \pm 1.45	2.67 \pm 1.50	ns
Difference of circumference, calf, day 9	0.03 \pm 0.92	0.90 \pm 1.28	2.30 \pm 1.53	A/C, $P < .001$, B/C, $P < .001$, A/B, $P < .01$
Clinical score, day 0	17.0 \pm 3.4	19.3 \pm 2.5	18.9 \pm 3.7	ns
Clinical score, day 9	7.7 \pm 1.2	9.5 \pm 1.9	12.1 \pm 3.9	A/C, $P < .001$, B/C, $P < .01$, A/B, $P < .05$
High probability scan, day 0	12	9	9	ns
New PEs, day 9	2	1	1	ns
Thrombus diameter, day 0	9.4 \pm 2.3	10.3 \pm 2.5	11.0 \pm 4.2	ns
Thrombus diameter, day 9	8.1 \pm 2.2	9.1 \pm 2.4	8.9 \pm 3.5	ns

ns, Not significant; PE, pulmonary emboli; V/Q, ventilation-perfusion.

ent in the three groups. No clinical, life-threatening, or fatal emboli were observed in the study.

An interesting trend was seen in the duplex scan findings, which, we think, has to be proved by a larger series. Because of the problem of exactly defining the proximal tip of the thrombus in cases of thrombi extending proximal to the inguinal fold, only patients with femoral vein involvement were evaluated. Progression and extension of the thrombus were more frequently observed in the bed rest group.

External leg compression has several physical effects, which have been measured in different experiments. It counteracts edema formation and leads to a narrowing of superficial and deep veins, which is demonstrated with phlebography. Inelastic material such as zinc plaster is more effective than elastic material for the reduction of local blood volume.¹⁶ Blood flow velocity increases, even when a patient is in the supine position and is wearing thromboprophylactic stockings of low pressure.¹⁷ It must be stressed that all positive effects of compression are tightly connected with the intentional and aggressive walking exercises that those patients were encouraged to perform. The rhythmic acceleration of venous flow velocity with every step is certainly a very potent mechanism to prevent venous stasis from promoting propagation of thrombi. Compression and early ambulation are accepted as effective measures in primary prevention, but they have been totally neglected or underestimated as very potent tools of therapy in the acute phase of DVT.

Thrombus propagation is observed in about 20% of patients, despite adequate heparin treatment if patients are mobilized after several days, but only in 1% if early ambulation is instituted.¹⁸ Hull et al¹⁹ have shown that prolonging the partial thromboplastin time to at least twice the control value with intravenous heparin within 24 hours is critical in preventing thrombus propagation. Thrombus propagation depends on the level of anticoagulation and is certainly also influenced by the amount of stasis, especially in this crucial time. Therefore, we consider mobilization of the patient with DVT immediately after diagnosis and application of LMWH essential and not 24 hours later.

Forty-four patients in this study, including 11 patients with pelvic and two with caval thrombosis, were treated in the hospital; one was treated on a daycare basis. During the study period of 9 days, no severe events were observed. The proposed treatment regimen of LMWH, compression, and walking exercises could also have been performed on an outpatient basis without any loss of quality. The economic advantages of complete or partial outpatient treatment are evident and will gradually change the current concept of hospital treatment of DVT.²⁰ However, clear guidelines concerning selection of patients for hospital or home therapy are needed.²¹ We conclude from this study that compression and walking in mobile patients with DVT lead to a faster reduction of leg swelling and pain without an increased risk of pulmonary embolism and should therefore replace the old tradition of bed rest.

REFERENCES

1. Koopman MMW, Prandoni P, Piovello F, Ockelford PA, Brandjes DPM, van der Meer J, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low-molecular-weight heparin administered at home. *N Engl J Med* 1996;334:682-7.
2. Levine M, Gent M, Hirsh J, Leclerc J, Anderson D, Weitz J, et al. A comparison of low-molecular-weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep-vein thrombosis. *N Engl J Med* 1996;334:677-81.
3. Partsch H, Oburger K, Mostbeck A, König B, Köhn H. Frequency of pulmonary embolism in ambulant patients with pelvic vein thrombosis: a prospective study. *J Vasc Surg* 1992;16:715-22.
4. Partsch H, Kechavarz B, Mostbeck A, Köhn H, Lipp C. Frequency of pulmonary embolism in patients who have iliofemoral deep vein thrombosis and are treated with once- or twice-daily low-molecular-weight heparin. *J Vasc Surg* 1996;24:774-82.
5. Partsch H, Kechavarz B, Köhn H, Mostbeck A. The effect of mobilization of patients during treatment of thromboembolic disorders with low-molecular-weight heparin. *Int Angiol* 1997;16:189-92.
6. Aschwanden M, Labs KH, Engel H, Müller J, Jeanneret CB, Jäger KA. Lungenembolien bei mobilisierten und immobilisierten Patienten mit proximaler tiefer Venenthrombose [abstract]. *Vasa* 1999;28:224.
7. Schellong SM, Schwarz TH, Krapp J, Prwescher Y, Beuthien-Baumann B, Daniel WG. Bed rest in deep vein thrombosis and the incidence of scintigraphic pulmonary embolism. *Thromb Haemost* 1999;82:127-9.
8. Lowenberg RL. Early diagnosis of phlebothrombosis with the aid of a new clinical test. *JAMA* 1954;155:1566-7.
9. Blättler W, Borer M, Linder C, Bergan J. Outpatient and conventional treatment of acute deep-vein thrombosis evaluated in a controlled single-center study. *Phlebologie* 1998;51:41-6.
10. Frank D, Blättler W. Comparison of ambulatory and inpatient treatment of acute deep venous thrombosis of the leg: subjective and economic aspects. *Schweiz Med Wochenschr* 1998;128:1328-33.
11. The Columbus Investigators. Low-molecular-weight heparin in the treatment of patients with venous thromboembolism. *N Engl J Med* 1997;337:657-62.
12. Wells PS, Kovacs MJ, Bormanis J, Forgie MA, Goudie D, Morrow B, et al. Expanding eligibility for outpatient treatment of deep venous thrombosis and pulmonary embolism with low-molecular-weight heparin: a comparison of patient self-injection with home-care injection. *Arch Intern Med* 1998;158:1809-12.
13. Brandjes PM, Büller HR, Heijboer H, Huisman MV, de Rijk M, Jagt H, et al. Incidence of the post-thrombotic syndrome and the effects of compression stockings in patients with proximal venous thrombosis. *Lancet* 1997;349:759-62.
14. Fischer H. Eine neue Therapie der Phlebitis. *Med Klin* 1910;30:1172-80.
15. Partsch H. Compression therapy of the legs. *J Dermatol Surg Oncol* 1991;17:799-805.
16. Partsch H, Menzinger G, Mostbeck A. Inelastic leg compression is more effective to reduce deep venous refluxes than elastic bandages. *Dermatol Surg* 1999;25:695-700.
17. Partsch H, Kahn P. Venöse Strömungsbeschleunigung in Bein und Becken durch Anti-Thrombose-Strümpfe. *Klinikarzt* 1982;11:609-15.
18. Schulman S. Studies on the medical treatment of deep vein thrombosis. *Acta Med Scand* 1988;224:Suppl 704.
19. Hull RD, Raskob GE, Hirsh J, Jay RM, Leclerc JR, Geerts WH, et al. Continuous intravenous heparin compared with intermittent subcutaneous heparin in the initial treatment of proximal-vein thrombosis. *N Engl J Med* 1986;315:1109-14.
20. Hull RD, Pineo GF, Raskob GE. The economic impact of treating deep vein thrombosis with low-molecular-weight heparin: outcome of therapy and health economy aspects. *Haemostasis* 1998;28 Suppl 3:8-16.
21. Yusen RD, Haraden BM, Gage BF, Woodward RS, Rubin BG, Botney MD. Criteria for outpatient management of proximal lower extremity deep venous thrombosis. *Chest* 1999;115:972-9.

Submitted Feb 17, 2000; accepted Apr 6, 2000.

DISCUSSION

Dr John A. Heit (Rochester, Minn). I congratulate Professor Partsch and colleagues on a well-designed study. The strengths of the study can be summarized as follows. The study objective addressed a relevant clinical problem, and the study design was a randomized clinical trial. The study methods included objective diagnostic testing for acute proximal deep vein thrombosis, appropriate inclusion and exclusion criteria, and anticoagulation therapy that is the current standard of care. The study interventions included the current standard of care in Europe (hospitalization with bed rest) as well as two additional groups (ie, Unna boot and graduated compression stocking therapy), which reflected more recent trends in care (eg, ambulatory outpatient LMWH therapy). The primary study end points of change in pain (as measured by a visual analogue scale and the Lowenberg test) and change in leg circumference were objective and quantifiable. However, the "clinical scores" were subjective and therefore must be interpreted

with caution since the study was not blinded. Measured walking distance was significantly greater for the Unna boot and the compression stocking groups compared with the bed rest group. Finally, the randomization appears to have been successful, and the primary end points were consistent and in favor of ambulation with either Unna boot or compression stocking therapy over bed rest.

The weaknesses of the study are as follows. Only about one third (45/148) of eligible patients were enrolled. The low enrollment could affect the generalizability of the study conclusions. To address this issue, the authors should provide additional information about the 103 patients who did not participate. The authors should also provide more information on how the graduated compression stockings were fitted. Were the stockings fitted based on measurements of the unaffected leg? Finally, the authors should include the duplex ultrasound and ventilation perfusion lung scan methods and the interpretation criteria. Were

lung scans interpreted as diagnostic of pulmonary embolism only if the scan was a "high probability" scan? What were the criteria for diagnosing a "new" pulmonary embolism? The authors found that the three groups did not differ significantly in the rate of proximal thrombus propagation or change in thrombus size (as measured by serial duplex ultrasounds), or evidence of new pulmonary embolism (as measured by serial lung scans). This finding should be interpreted with caution because the sample size was too small to exclude a significant difference.

In summary, I believe the authors' major conclusions are correct. Moreover, the conclusions are supported by at least two other large randomized clinical trials (Koopman 1996, Levine 1996) and a recent cohort study (Wells 1998). I urge the authors to enlarge the sample size and include a longer duration of clinical follow-up. I also urge the authors to determine the cumulative incidence of venous stasis syndrome (VSS) among the three intervention groups. Although one trial found that compression stocking therapy reduced the 2-year cumulative incidence of VSS, 20% of patients receiving compression stockings still developed mild to moderate VSS (Brandjes 1997). However, compression stocking therapy was delayed for 2 to 3 weeks. "Immediate" compression therapy, as performed in this study, may further reduce the incidence of VSS.

Dr Hugo Partsch. Thank you very much Dr Heit for your very valuable comments and for your kind words. To answer your questions:

First, what happened to the other patients who were not included in this study? These were patients who were

treated the same way as we do it now for about 30 years already. All these patients are admitted to our ward, they get anticoagulation, and they remain walking. Since our institution has become popular for not putting patients into bed, this was also the reason why we were able only to find 45 patients who accepted the risk of being put into bed by randomization.

Your second question concerning the stocking: the stocking was adopted to the involved leg, not to the opposite leg, and the stocking stayed on these patients overnight.

Concerning perfusion ventilation lung scan, yes, our sample size was much too small to get any kind of information out of that, but several times we have published our findings of ventilation perfusion scanning in more than 1000 patients now, before, and after 9 days of our kind of treatment, not putting patients into bed. Comparing these data with the literature there is no significant difference. As I have mentioned there is one study from Basle and one from Schellong in Germany where the patients were randomized into a bed rest group and a walking group. The authors were also not able to find higher frequency of pulmonary embolism in walking patients compared with bed rest patients.

Your fourth point was if we would like to extend the study. Yes, certainly this would be a good idea because there may be some difference also concerning the development of post-thrombotic syndrome. As you have mentioned in the study from Brandjes, the patients started to be treated with stockings only after 9 days.

Thank you very much for your comments.